1. Applicant's election with traverse of Group I, claims 1-50, 54-63, and 75, in the reply filed on 04/25/08 is acknowledged. The traversal is on the ground(s) that the burden placed on Applicants in having to file and prosecute separate applications for the inventions of Groups I, II, II, IV, and V outweighs the burden placed on the Examiner in searching the inventions of these groups together. This is not found persuasive because it does not address the criteria of the restriction, which is based on lack of unity of invention under PCT Rules 13.1 and 13.2.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 51-53, 64-74, and 76-78 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 04/25/08.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

4. Claims 24 and 47 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must refer to prior claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-23, 25-46, 48-50, 54-63, and 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) These claims are confusing because it is unclear what is encompassed by “unpaired regions” in independent claim 1. This might be reasonably interpreted by the skilled artisan to encompass a “mismatch”, although it is unclear if this is an embodiment intended in the specification. It is suggested that “loop” be used in amended claims rather than "unpaired region", as it is believed that this more clearly defines the disclosed invention. Clarification is required.

B) Claim 10 is confusing because “tag complex” and “the tag” lack proper antecedent basis. Correction is required.

C) Claim 11 is confusing because it cannot be determined what is encompassed by a "chemical group" or "chemical substance". Clarification is required.

D) Claim 12 is confusing because "the tag" lacks proper antecedent basis. Correction is required.

E) Claim 15 is confusing because "the tag" lacks proper antecedent basis, and it is unclear what the meaning of "and/or chemical matrix" is. Correction is required.

F) Claim 16 is confusing because "the tag" lacks proper antecedent basis, a word is missing after "digoxigenin", and there is no period at the end. Correction is required.

G) Claim 17 is confusing because "the tag" lacks proper antecedent basis. Correction is required.

H) Claims 18 and 19 are confusing because "the matrix" lacks proper antecedent basis. Correction is required.

I) Claim 28 is confusing because "as recovered at step a), b), c) and/or d) of claim 1" is not consistent with what is recited in claim 1.

J) Claim 29 is confusing because "the obtained libraries" lacks proper antecedent basis. Correction is required.

K) Claim 35 is confusing because it cannot be determined what is encompassed by "the whole sequence of an unpaired region". Clarification is required.

L) Claim 42 is confusing because it is not a complete sentence, and lacks a period at the end. Correction is required.

M) Claim 43 is confusing because of the language "wherein the in step". Correction is required.

N) Claim 50 is confusing because "the isoform" (singlular) lacks proper antecedent basis, and also it cannot be determined what is encompassed by "substantially comprises the unpaired region". Clarification is required.

O) Claim 55 is confusing because it cannot be determined what active step(s) is/are required by "using the information obtained according to the method of claim 1". Clarification is required.

P) Claim 56 is confusing because the letter headings "l", "m", and "n" do not follow prior headings ending in "k". Clarification is required.

Q) Claim 59 is confusing because it is unclear how the method further limits claim 1. Clarification is required.

R) Claim 60 is confusing because "the sequence information" lacks proper antecedent basis, and it is unclear how the method further limits claim 1. Correction is required.

S) Claim 61 is confusing because "the obtained isoform sequencing data" lacks proper antecedent basis, and it is unclear how the method further limits claim 1. Correction is required.

T) Claim 63 is confusing because it is unclear how the method further limits claim 1. Clarification is required.

U) Claim 75 is confusing because it is unclear how the method further limits claim 1. Clarification is required.

6) The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Huo (US 5,922,535).

This claim is drawn to a method comprising: preparing at least two nucleic acid isoforms; hybridizing the isoforms and forming double-stranded RNA/RNA or DNA/DNA hybrids comprising unpaired or loop regions; recovering such hybrids comprising unpaired or loop regions from other nucleic acids; and identifying, analyzing, and/or cloning such recovered hybrids.

Huo discloses such a method; see Fig. 3 and column 22, line 34 to column 23, line 10.

8.) Claims 1-4, 8-20, 25-46, 48-50, 54-63, and 75 are rejected under 35 U.S.C. 102(b) as being anticipated by Thill (WO 02/31190).

Thill discloses the claimed methods; see Figs. 1 and 8; pages 3-8, 10-11, 23-24, 27-29, 34-40, and 42-49. Specifically, the use of restriction enzymes is disclosed on page 24, and the use of exonuclease (Exo) VII is disclosed on page 27. The methods as claimed cannot be distinguished from the disclosure of Thill.

9. Claims 1, 2, 4, 6-20, 25-46, 48-50, 54-63, and 75 are rejected under 35 U.S.C. 102(e) as being anticipated by Schweighoffer et al. (US 6,881,571, 11/30/2000).

Schweighoffer et al. disclose the claimed methods; see especially Fig. 6A and column 8, line 51 to column 9, line 52; also see column 9, line 63 to column 27. The use of the restriction enzyme Sau3AI is taught, for example, in Fig. 6A.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5-7 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thill in view of Kwon et al.

These claims are drawn to the method as discussed and rejected above, further comprising the use of restriction enzymes having a 4 bp recognition site and Y-shaped linkers.

Although Thill does not disclose the further teachings, these are taught as useful in cloning/amplifying nucleic acids by Kwon et al. (see pages 195-199, especially Fig. 1 which shows a Y-shaped linker, and the restriction enzyme Nla III).

One of ordinary skill in the art would have been motivated to use a restriction enzyme having a 4 bp recognition site, and a Y-shaped linker, in the method of Thill because Kwon et al. taught that these reagents were known in the art to be useful in nucleic acid cloning and amplification. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods.

11. No claims are free of the prior art.

12. Thill (US 6,632,610), an equivalent of Thill (WO 02/31190), is made of record as a reference of interest.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kenneth R. Horlick whose telephone number is 571-272-0784. The examiner can normally be reached on Monday-Thursday 6:30AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

06/16/08